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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/956,991	10/23/1997	JULIE R. KORENBERG	P-CE-2817	9464

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/956,991	KORENBERG, JULIE R.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,13-19,21-29,31,32,38-46 and 48* is/are pending in the application.

4a) Of the above claim(s) *11 and 21-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 31-32, 38-46 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/04 has been entered.

2. Claims 1, 11, 13-19, 21-29, 31-32, 38-46, and 48 are pending. Claims 11 and 21-29 are withdrawn from prosecution as being drawn to non-elected inventions. As a formal matter, applicant is advised that the amendment filed 5/19/04 was not fully compliant with rule 1.121 because the full text of the withdrawn claims was not recited. In the interest of compact prosecution the amendment was considered, but applicant is advised that future amendments should recite the withdrawn claims as required by 37 CFR 1.121(c).

3. Claims 1, 31-32, 38-46 and 48 are examined herein.

4. The previously set forth 112 1st paragraph rejection of claims 33-37 and 49 are moot in view of applicant's cancellation of these claims.

Claim Rejections - 35 USC § 101

5. The rejection of claims 1 and 31-46 and 48-49 under 35 U.S.C. 101 and 112 1st because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility is WITHDRAWN in view of the declaration and arguments filed 5/19/04. The declaration establishes that in view of the teachings of the specification and

the prior art the instantly claimed invention has at least a specific, substantial, and credible utility in that the nucleic acid molecules can be used for diagnosing a predisposition for Downs syndrome phenotype.

However, in view of the establishment of a this utility under 101, there are further issues to be considered with regard to the scope of enablement of the claims. A new grounds of rejection follows.

Claim Rejections - 35 USC § 112

6. Claims 1, 31, 32, 38, 39, 40, 41, 42, 43, 44, 45, 46, and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid consisting of an isolated nucleic acid molecule consisting of the nucleotide sequence set forth in SEQ ID NO: 1 or in SEQ ID NO: 11, or an oligonucleotide consisting of at least 50 contiguous nucleotides of one of these, or the full length complement of one of these, does not reasonably provide enablement for all nucleic acids encoding one of SEQ ID NO: 2 or 11 or all nucleic acids which are fragments of these or isolated nucleic acid molecules consisting of SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID NO: 9, or fragments of these. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to isolated nucleic acid and oligonucleotide molecules as well as vectors, host cells, and kits comprising the same. During prosecution history a 101 rejection was set forth for lack of utility, and applicant has argued and provided a declaration to establish that a utility for the claimed invention is as a nucleic acid probe marker for Down syndrome phenotype in humans (see at least most recent response by applicant). Thus, the

nature of the invention is reliant upon the ability of the claimed nucleic acids to hybridize to the marker sequence.

Claim 1 is drawn to an isolated nucleic acid consisting essentially of a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 11 or the complement of one of these. The claim is quite broad in nature due to the degeneracy of the human genome, where each individual amino acid can be encoded by as many as four different codons. Therefore, the scope of the claim allows for a sequence change relative to the disclosed SEQ ID NO: 1 or SEQ ID NO: 10 of approximately every third nucleotide across the entire molecule. Claims 31 and 32 depend from claim 1 and recite a vector and host cell comprising the sequence of claim 1. Claim 48 recites that the isolated nucleic acid of claim 1 is RNA.

Claim 38 is drawn to an isolated nucleic acid consisting of a nucleotide sequence which encodes a nucleotide sequence which encodes a polypeptide comprising at least one of a series of fragments of SEQ ID NO: 2 that are recited in the claim. The claim is quite broad in nature due to the degeneracy of the human genome, where each individual amino acid can be encoded by as many as four different codons. Therefore, the scope of the claim allows for a sequence change relative to the disclosed SEQ ID NO: 1 or SEQ ID NO: 10 of approximately every third nucleotide across the entire molecule. Additionally, the claim is broad in nature because it is drawn using open claim language- the nucleic acid must encode a polypeptide that COMPRISES a particular polypeptide, which encompasses nucleic acids that encode any number of variants (for example, allelic and splice variants as well as polypeptides potentially from other organisms) as well as nucleic acids which encode any possible amino acid sequences that flank the recited

fragments. Claims 39 and 40 depend from claim 38 and recite a vector and a host cell containing the nucleic acid of claim 38.

Claim 41 is drawn to an isolated nucleic acid molecule consisting of the nucleotide sequence set forth in SEQ ID NO: 1, SEQ ID NO: 10, nucleotides 453-6185 of SEQ ID NO: 1, or nucleotides 453-5168 of SEQ ID NO: 10, or the complement of one of these. These embodiments of claim 41, as well as vectors and cells comprising the same are within the scope of the enabled invention. Claim 41 also includes an isolated nucleic acid molecule consisting of the nucleotide sequence set forth in SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID NO: 9, or the complement of one of these. These sequences are the 5', middle and 3' portions of a gene which encodes a putative murine "DS-CAM" molecule. Claims 42 and 43 depend from claim 41.

Claim 44 is drawn to an oligonucleotide consisting of at least 50 nucleotides of a nucleotide sequence that encodes amino acids 1 to 1473 of SEQ ID NO: 11 or at least 50 nucleotides of the sequence set forth in SEQ ID NO: 7 and SEQ ID NO: 8, or the complement of on of these. Claim 45 recites that the oligonucleotide of claim 44 consists essentially of SEQ ID NO: 5 or SEQ ID NO: 6. Claim 46 recites a kit which comprises the oligonucleotide of claim 44 or 45.

The specification discloses that the nucleic acids of SEQ ID NO:1 and SEQ ID NO:11 are transcribed in neural crest cells, that the gene responsible for these coding sequences is localized to a region of chromosome 21 associated with Down Syndrome (21q22.2-22.3), and that the encoded polypeptide is a neural cell adhesion molecule based upon its structural homology with other neural adhesion molecules and its expression pattern (e.g., on pages 9-11, 43-44 and 56-62). The specification further teaches that SEQ ID NO: 7, SEQ ID NO: 8, and

SEQ ID NO: 9 are partial cDNA clones isolated from mice using human DS-CAM cDNA clone as a probe.

The specification does not teach how to use the claimed nucleic acids commensurate in scope with the breadth of the claims because the specification does not provide any guidance as to how SEQ ID NO: 1 and SEQ ID NO: 11 can be modified but still retain their ability to hybridize to the region of human chromosome 21 that is associated with Downs syndrome. In the instant case, the functionality of the claimed invention is based on a linear sequence necessary for the detection of a target, yet the claim encompasses hundreds of thousands of variants that may or may not be useful for this purpose. The specification does not provide any discussion or guidance as to which portions of SEQ ID NO: 1 or SEQ ID NO: 11 can be modified yet still retain their ability to serve as a marker linked with DS phenotype. The degeneracy of the genetic code is such that any single amino acid is encoded for by at least two but as many as four different codons, and it is unpredictable which of these from within this large genus would be useful for the detection of the DS phenotype. The changing of every third nucleotide along a linear sequence would drastically change the internal hybridization specificity of the nucleotide to be used as a hybridization probe, for example. With regard to SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, and fragments thereof, the specification does not teach or suggest how these would be useful for the detection of human Downs syndrome phenotype, nor does the specification provide any guidance or working examples for the detection of this phenotype in mice.

The specification does not provide any working examples wherein DS phenotype or any other phenotype is detected using nucleic acid sequences which differ from instant SEQ ID NO:

1 or SEQ ID NO: 10 or which are murine sequences. In order to practice the claimed invention commensurate in scope with the claims, one would be required to produce hundreds of thousands of possible variants of instant SEQ ID NO: 1 and SEQ ID NO: 10 and establish in patient populations that they indeed are useful for the detection of DS phenotype. Further, with regard to claims that encompass murine sequences, one would have to undertake extensive experimentation to establish a link between this sequence which may or may not be causative of DS phenotype. Though the specification teaches that the human DS-CAM is on a region of the genome that is linked to DS phenotype, it has not established that this molecule is causative. Therefore, it can not be extrapolated that a related molecule in a different organism would also be linked to the phenotype or useful for detecting the phenotype in humans or in other animals.

Thus, in light of these factors, it is concluded that it would require undue experimentation to use the claimed invention commensurate in scope with these claims.

Conclusion

7. There is no allowable claim. The claims are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this

application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Examiner
Art Unit 1634

July 29, 2004